DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service P930035

# Memorandum

Date MAR 10 1995

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Cardiac Pacemakers, Inc., VENTAK® P2 AICD™ System, Model 1625 VENTAK® P2 Pulse Generator, Model 2835 Software Module, Model 2815 VENTAK® ECD External Cardioverter Defibrillator - ACTION

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

Prepared by CDRH, HRZ-450. (CCAREY, 2/10/95), 443-8609

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

[DOCKET NO. _____]

Cardiac Pacemakers, Inc., PREMARKET APPROVAL OF VENTAK® P2 AICD™ SYSTEM: MODEL 1625 VENTAK® P2 PULSE GENERATOR, MODEL 2835 SOFTWARE MODULE, and MODEL 2815 VENTAK® ECD EXTERNAL CARDIOVERTER DEFIBRILLATOR

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Cardiac Pacemakers, Inc., St. Paul MN, for premarket approval, under section 515 of the Federal Food, Drug, and Cosmetic Act (the act), of the VENTAK® P2 AICD™ System.

FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on _____, of the approval of the application.

DATE: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER)

ADDRESS: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 1-23, 12420 Parklawn Drive, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Carole Carey

Center for Devices and Radiological Health (HFZ-450)

Food and Drug Administration

9200 Corporate Blvd.

Rockville, MD 20850

301-443-8609.

SUPPLEMENTARY INFORMATION: On August 30, 1993, Cardiac Pacemakers, Inc., St. Paul, MN 55112, submitted to CDRH an application for premarket approval of VENTAK® P2 AICD™ System consists of the following: Model 1625 VENTAK® P2 pulse generator; Model 2835 Software Module to be used with commercially available Cardiac Pacemakers, Inc. (CPI®) Model 2035 Handheld Programmer and Model 6575 or 6577 Telemetry Wand; Model 2815 VENTAK® ECD External Cardioverter Defibrillator (which includes the Model 6873 High Voltage Cable with Model 6838 Thumbscrew, Model 6843 Bipolar Cable with Model 6838 Thumbscrew, Model 6874 Bipolar Cable, and related CPI® commercially available accessories); commercially available CPI® ENDOTAK® 60-Series Lead System and accessories; commercially available CPI® epicardial defibrillation leads and accessories; and commercially available pace/sense leads and accessories. The device is an automatic implantable cardioverter defibrillator system and is indicated for the treatment of patients with ventricular fibrillation and/or ventricular tachyarrhythmias who are at high risk of sudden cardiac death. Such patients are defined as having experienced the following situations: (1) the survival of at least one episode of cardiac arrest presumably due to hemodynamically unstable ventricular tachyarrhythmia not associated with acute myocardial infarction, and/or (2) a poorly tolerated, sustained ventricular

tachycardia (VT) and/or ventricular fibrillation (VF) which recurs spontaneously or can be induced despite the best antiarrhythmic drug therapy. *Note: The clinical outcome of hemodynamically stable, sustained VT patients is not fully known. A study of the safety and effectiveness of the VENTAK® P2 system on this selected subgroup of VT patients has not been conducted.*

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory panel, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

On _____, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

## OPPORTUNITY FOR ADMINISTRATIVE REVIEW

Section 515(d)(3) of the act (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act (21 U.S.C. 360e(g)), for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. This notice is issued under the Federal Food, Drug, and Cosmetic Act section 520(h), 90 Stat. 554-555, 571 (21 U.S.C. 360e(d), 360j(h)) and under authority

delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: _____.

_____

D. Bruce Burlington, M.D.
Director
Center for Devices and
Radiological Health

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL

_____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Ann Quinlan Smith
Senior Regulatory Affairs Associate
Cardiac Pacemakers, Inc.
4100 Hamline Avenue North
St. Paul, Minnesota 55112-5798

MAR 10 1995

Re: P930035
VENTAK® P2 AICD System
Model 1625 VENTAK® P2 Pulse Generator
Model 2835 Software Module
Model 2815 VENTAK® ECD External Cardioverter Defibrillator
Filed: August 30, 1993
Amended: September 23 and December 27, 1993, June 24, July 15, September 14, September 23, October 17, and November 21, 1994, January 25, and March 6, 1995

Dear Ms. Smith:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the VENTAK® P2 AICD™ System: Model 1625 VENTAK® P2 pulse generator; Model 2835 Software Module to be used with commercially available Cardiac Pacemakers, Inc. (CPI®) Model 2035 Handheld Programmer and Model 6575 or 6577 Telemetry Wand; Model 2815 VENTAK® ECD External Cardioverter Defibrillator (which includes the Model 6873 High Voltage Cable with Model 6838 Thumbscrew, Model 6843 Bipolar Cable with Model 6838 Thumbscrew, Model 6874 Bipolar Cable, and related CPI® commercially available accessories); commercially available CPI® ENDOTAK® 60-Series Lead System and accessories; commercially available CPI® epicardial defibrillation leads and accessories; and commercially available pace/sense leads and accessories.

This device is indicated for the treatment of patients with ventricular fibrillation and/or ventricular tachyarrhythmias who are at high risk of sudden cardiac death. Such patients are defined as having experienced the following situations: (1) the survival of at least one episode of cardiac arrest presumably due to hemodynamically unstable ventricular tachyarrhythmia not associated with acute myocardial infarction, and/or (2) a poorly tolerated, sustained ventricular tachycardia (VT) and/or ventricular fibrillation (VF) which recurs spontaneously or can be induced despite the best antiarrhythmic drug therapy. *Note: The clinical outcome of hemodynamically stable, sustained VT patients is not fully known. A study of the safety and effectiveness of the VENTAK® P2 system on this selected subgroup of VT patients has not been conducted.* We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval for Implantable Defibrillators and Programmers" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the following information until such time that adequate justification to cease reporting the information is submitted to FDA: (1) updated life testing conducted on the pulse generator's power source (battery) and high energy capacitors; (2) updated details of any patients with devices confirmed to exhibit digital hybrid damage due to electrical overstress resulting from the piezo attachment process; (3) updated calculations of device longevity based on further clinical experience; and, (4) updated analysis of survival for patients programmed with 'VF Protection' ON and OFF.

Expiration dating for this device has been established and approved at 1 year shelf life. The storage temperature is between 0° - 50°C (32° - 122°F).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that as soon as possible, and before commercial distribution of your device, that you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

In addition under section 522(a) of the act, manufacturers of certain types of devices identified by the act or designated by FDA are required to conduct postmarket surveillance studies. FDA has identified under section 522(a)(1)(A) the above noted device as requiring postmarket surveillance.

Upon approval and within thirty (30) days of first introduction or delivery for introduction of this device into interstate commerce you will be required to submit to FDA certification of the date of introduction into interstate commerce, a detailed protocol which describes the postmarket surveillance study, and a detailed profile of the study's principal investigator that clearly establishes the qualifications and experience of the individual to conduct the proposed study. For your information, general guidance on preparing a protocol for a postmarket surveillance study is enclosed. At that time you should submit five (5) copies to:

Postmarket Studies Document Center
1350 Piccard Drive (HFZ-544)
Rockville, Maryland 20850

Within sixty (60) days of receipt of your protocol, FDA will either approve or disapprove it and notify you of the Agency's action in writing. Do not undertake a postmarket surveillance study without an FDA approved protocol.

Failure to certify accurately the date of initial introduction of your device into interstate commerce, to submit timely an acceptable protocol, or to undertake and complete an FDA approved postmarket surveillance study consistent with the protocol, will be considered violations of section 522. In accordance with the Medical Device Amendments of 1992, failure of a manufacturer to meet its obligations under section 522 is a prohibited act under section 301(q)(1)(C) of the act (21 U.S.C. 331(q)(1)(C)). Further, under section 502(t)(3) of the act (21 U.S.C. 352(t)(3), a device is misbranded if there is a failure or refusal to comply with any requirement under section 522 of the act. Violations of sections 301 or 502 may lead to regulatory actions including seizure of your product, injunction, prosecution, or civil money penalties or other FDA enforcement actions including (but not limited to) withdrawal of your PMA.

If you have any questions concerning postmarket surveillance study requirements, contact the Postmarket Surveillance Studies Branch, at (301) 594-0639.

Under section 519(e) of the act (as amended by the Safe Medical Devices Act in 1990), manufacturers of certain devices must track their products to the final user or patient so that devices can be located quickly if serious problems are occurring with the products. The tracking requirements apply to (1) permanent implants the failure of which would be reasonably likely to have serious adverse health consequences; (2) life sustaining or life supporting devices that are used outside of device user facilities the failure of which would be reasonably likely to have serious adverse health consequences; and (3) other devices that FDA has designated as requiring tracking. Under section 519(e), FDA believes that your device is a device that is subject to tracking because

it is a permanent implant whose failure would be reasonably likely to have serious adverse consequences. FDA has designated your device for tracking.

FDA's tracking regulations, published in the FEDERAL REGISTER on August 16, 1993, appear at 21 CFR Part 821. These regulations set out what you must do to track a device. In addition, the regulations list example permanent implant and life sustaining or life supporting devices that FDA believes must be tracked at 21 CFR § 821.20(b) and the devices that FDA has designated for tracking at 21 CFR § 821.20(c). FDA's rationale for identifying these devices is set out in the FEDERAL REGISTER (57 FR 10705-10709 (March 27, 1991), 57 FR 22973-22975 (May 29, 1992), and 58 FR 43451-43455 (August 16, 1993)).

If you have questions concerning this approval order, please contact Carole Carey at (301) 443-8609.

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosures

# SUMMARY OF SAFETY AND EFFECTIVENESS DATA

VENTAK® P2 AICD™ System

(P930035)

Food and Drug Administration • Center for Devices and Radiological Health • Office of Device and Evaluation
Division of Cardiovascular Respiratory and Neurological Devices

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## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### I. GENERAL INFORMATION

| | |
|---|---|
| Device Generic Name: | Automatic Implantable Cardioverter Defibrillator System, Program Disk, External Cardioverter Defibrillator |
| Device Trade Names: | VENTAK® P2 AICD™ System:<br>Model 1625 VENTAK® P2 Pulse Generator<br>Model 2835 Software Module<br>Model 2815 VENTAK® ECD External Cardioverter Defibrillator |
| Applicant's Name and Address: | Cardiac Pacemakers, Inc. (CPI®)<br>4100 Hamline Ave. North<br>St. Paul, MN 55112-5798 |
| PMA Number: | P930035 |
| Date of Notice of Approval to Applicant: | March 10, 1995 |

### II. INDICATIONS FOR USE

The VENTAK® P2 AICD™ (Automatic Implantable Cardioverter Defibrillator) system, with the Model 1625 VENTAK® P2 pulse generator, cardioversion and defibrillation leads and accessories is intended for use in the treatment of patients with ventricular fibrillation and/or ventricular tachyarrhythmias who are at high risk of sudden cardiac death. Such patients are defined as having experienced the following situations: (1) the survival of at least one episode of cardiac arrest presumably due to hemodynamically unstable ventricular tachyarrhythmia not associated with acute myocardial infarction, and/or (2) a poorly tolerated, sustained ventricular tachycardia (VT) and/or ventricular fibrillation (VF) that recurs spontaneously, or can be induced despite the best antiarrhythmic drug therapy.

*NOTE: The clinical outcome of hemodynamically stable, sustained-VT patients is not fully known. A study of the safety and effectiveness of the VENTAK P2 system on this selected subgroup of VT patients has not been conducted.*

### III. DEVICE DESCRIPTION

The VENTAK® P2 AICD System consists of the following: Model 1625 VENTAK P2 pulse generator; Model 2835 Software Module to be used with commercially available CPI® Model 2035 Handheld Programmer and Model 6575 or 6577 Telemetry Wand; Model 2815 VENTAK® ECD External Cardioverter Defibrillator (which includes the Model 6873 High Voltage Cable with Model 6838 Thumbscrew, Model 6843 Bipolar Cable with Model 6838 Thumbscrew, Model 6874 Bipolar Cable, and related CPI® commercially available accessories); commercially available CPI® ENDOTAK® 60-Series Lead System and accessories; commercially available CPI® epicardial defibrillation leads and accessories; and commercially available pace/sense leads and accessories.

#### A. Model 1625 VENTAK P2 Pulse Generator

The VENTAK P2 pulse generator contains an inner structure of discrete electrical components, interconnected hybrid circuit assemblies, batteries (two lithium silver vanadium oxide batteries), high-voltage capacitors, and a telemetry coil. There are nine leadless chip carriers used in the pulse generator. This inner assembly is enclosed in a hermetically sealed titanium case. A premolded polyurethane top is attached to the body for lead connection. The header has two 6.1 mm morphology-sensing and defibrillation lead ports and two 4.75 mm rate sensing and pacing lead ports. The VENTAK P2 pulse generator weighs approximately 233 grams with a volume of about 144 cc.

The VENTAK P2 pulse generator is a hybrid electrical device which is designed to provide defibrillation therapy (biphasic or monophasic shocks) as well as bradycardia pacing therapy. The pulse generator is capable of delivering low energy cardioversion (LEC) or high energy defibrillation shocks (HES). Bradycardia VVI (ventricular-demand mode) pacing is available for bradyarrhythmia management as well as to support the cardiac rhythm after defibrillation shock therapy. One additional programmable feature (committed or noncommitted shock) allows the pulse generator to check the rhythm during and after charging to ensure that the arrhythmia is sustained prior to therapy delivery. Another programmable feature (VF Protection) allows MVT (monomorphic ventricular tachycardia) to be treated with a programmable low first shock energy while ensuring that ventricular fibrillation (VF) will be treated with a high first-shock energy.

**Sensing and Detection**: Detection is based on cardiac cycle length (rate), with a programmable range of 110 - 220 bpm, in conjunction with a programmed duration. Duration is the time from recognition of an arrhythmia to initiation of charging for therapy delivery that is intended to ensure the arrhythmia is sustained. The pulse generator calculates rate on an interval-by-interval basis. Each cycle length is categorized as either bradycardia, normal sinus rhythm, tachycardia or fibrillation rate. The pulse generator is capable of classifying an arrhythmia as VT or VF based on the rate of the sensed tachyarrhythmia, if programmed by the physician (VF Protection feature). Duration is programmable in intervals between 2.5 and 10 seconds for a VT zone and fixed at 2.5 seconds for a VF zone. The timers for the VT window and VF window run independently and concurrently. The detection timer in the VF zone takes precedence over the VT duration timer regardless of which duration expires first to ensure that the most lethal rhythm is treated with a high first shock energy. The VENTAK P2 uses automatic gain control circuitry with a maximum sensitivity of 0.25 mV to sense tachyarrhythmias as well as bradyarrhythmias. When a paced pulse is delivered, the AGC (automatic gain control) sets the amplifier sensitivity at a fixed level during the paced refractory period.

**Therapy**: An arrhythmia that falls into the programmed heart rate range (VT or VF) will be managed by the energy required by that range. The first shock in a sequence treating VT rates is programmable from 0.1 - 34 joules; the remaining shocks in the sequence are nonprogrammable at 34 joules. When VF protection is enabled, all five shocks in a sequence treating VF rhythms are non-programmable at 34 joules. The type and polarity of the shock waveform are programmable. The waveform (biphasic or monophasic) determines how the pulse generator uses the energy on the capacitors. The waveform polarity reflects the relationship between voltages on the two defibrillating output leads. Converted rhythms are analyzed as to the need for bradycardia treatment. Following shock therapy, the VENTAK P2 pulse generator can provide high output pace pulses, if programmed. Standard VVI pacing is available for the treatment of bradycardia.

**Memory**: The VENTAK P2 pulse generator stores in memory the device's programmed parameters as well as model number, serial number, episode count, shock lead impedance, shocks delivered and diverted, and battery status. The VENTAK P2 also records and stores patient information surrounding each therapy episode/attempt. The device is capable of storing therapy detail of up to 69 single attempt episodes. For each episode, the device stores (1) the date and elapsed time; (2) attempt data that includes the number of therapy attempts; (3) shock energy level and shocking lead impedance of each attempt; (4) the detected heart rate; (5) the presence of stored electrograms; and, (6) reconfirmation results. Up to 2.5 minutes of electrograms surrounding the most recent episodes can be stored. The onset electrogram refers to the 10 seconds of signal prior to the initial detection window being satisfied. Pre-therapy storage provides up to 15 seconds of information starting with the beginning of duration and ending with therapy delivery (includes charge and reconfirmation times). Post-therapy storage starts following therapy delivery and stores 10 seconds of electrogram.

**Diagnostic Features**: The VENTAK P2 pulse generator provides the following diagnostic and optional features: (1) real-time electrogram and event markers which assist in evaluating system response; (2) non-invasive methods for inducing arrhythmias, including high rate pacing via the shocking leads and fixed rate, burst pacing via the

rate/sense leads; (3) automatic battery voltage evaluation every 24 hours; (4) automatic capacitor reformation every 60 days; (5) pacing lead impedance, calculated over 10 paced complexes, which can be used as a relative indicator of lead status over time; (6) battery status indicator displayed as one of five levels: Beginning of Life (BOL), Middle of Life (MOL1 and MOL2), Elective Replacement Indicator (ERI), and End of Life (EOL); (7) programmable audible tones (beeper function) which can be used to assist with system evaluation such as pulse generator battery status, capacitor charging, and rate sensing; (8) magnet control which can be programmed OFF to ensure the tachy mode will not be changed in the presence of a magnetic field, or programmed ON to allow the tachy mode of the pulse generator to be changed from INACTIVE or MONITOR ONLY mode to ACTIVE mode or from ACTIVE to INACTIVE mode. The magnet can also divert or inhibit therapy and enable the beeper.

**B. Model 2835 Software Module**

The Model 2835 Software Module, used in conjunction with the commercially available Model 2035 Handheld Programmer is used to program the VENTAK P2 pulse generator. It provides a variety of programmable options: the choice of one of three operational modes, one of two tachyarrhythmia management zones, bradycardia pacing, and combinations of bradycardia pacing and tachyarrhythmia therapies. The programmer system features a keyboard for entering commands, a liquid crystal display (LCD), a printer that provides a hard copy of selected data, and a built-in telemetry antenna for two-way RF radio frequency communication allowing interrogation and programming of all parameters and memory functions applicable to the VENTAK P2 pulse generator. The Model 6575 or 6577 Telemetry Wand can also be used to facilitate telemetry. Special functions such as STAT, STAT PACE, INTR, PROG, MENU, ASSIST, and DIVERT are accessible through the keyboard. The software module consists of a printed circuit board containing memory integrated circuits encased in a protective plastic housing that is physically compatible with a slot in the underside of the Model 2035 programmer.

**C. Model 2815 VENTAK ECD External Cardioverter Defibrillator**

The monophasic-biphasic Model 2815 VENTAK ECD is intended for use during the AICD implant procedure to establish cardiac arrhythmia conversion energy requirements and defibrillation thresholds, to evaluate arrhythmia detection rates and timing, to assess lead placement, and to provide any necessary back-up defibrillation during the intraoperative testing of the AICD pulse generator. The inner assembly of the Model 2815 VENTAK ECD includes printed circuit boards, a rechargeable battery, a hard-copy printer, and connector terminals for cable connections to implanted cardiac leads. The external case of the VENTAK ECD consists of injection molded plastic that serves as a housing for the device's internal components.

**D. Leads**

The lead systems for the VENTAK P2 AICD pulse generator are implanted using either transthoracic or transvenous techniques. In addition to the commercially available CPI ENDOTAK 60-Series Lead System, commercially available CPI epicardial defibrillation leads can also be used with the VENTAK P2 pulse generator. Lead connectors for all CPI 6.1 mm defibrillation leads and 4.75 mm rate sensing leads have been tested with the Model 1625 VENTAK P2 pulse generator.

## IV. CONTRAINDICATIONS

Use of the VENTAK P2 pulse generator is contraindicated for the following patients: (1) patients whose ventricular tachyarrhythmias may have reversible cause (such as digitalis toxicity, electrolyte imbalance, hypoxia, or sepsis) or whose ventricular tachyarrhythmias have a transient cause (such as, acute myocardial infarction, electrocution, or drowning, and (2) patients who have a unipolar pacemaker.

Note: A dedicated bipolar pacemaker is recommended. Refer to Appendix B in the Physician's Manual for information about required pacemaker/AICD interaction testing and procedures.

## V. WARNINGS

*General*

- For patients whose ventricular tachyarrhythmias require frequent shocks, the pulse generator batteries can deplete soon after implantation. In such a case, based on the patient's condition and history, use professional judgment to decide whether the expected benefits outweigh the possibility of early battery depletion necessitating device replacement.

- Drug-resistant supraventricular tachyarrhythmias (SVTs) in some patients can initiate unwanted therapy delivery by the VENTAK P2 pulse generator. Use professional judgment to determine if the device and programmable options are appropriate for these patients.

*AICD/Lead Compatibility*

- Use CPI leads with CPI AICD pulse generators. Refer to Appendix E (Physician's Manual) for a list of CPI leads used during the VENTAK P2 clinical investigation. No data are available on the performance of the VENTAK P2 pulse generator used with other manufacturers' epicardial or endocardial (transvenous) defibrillation lead systems. The potential adverse consequences of using such a combination may include, but are not limited to, undersensing cardiac activity and failure to deliver necessary therapy.

- Other rate-sensing leads were implanted during the clinical study and were found to be functionally compatible. Prior to the implantation of this pulse generator with other rate-sensing leads, confirm compatibility with the appropriate manufacturers' technical services department.

*Implantation Preparation*

- Improper use of the AICD system could damage or destroy the AICD system or other equipment, or result in injury to or death of the patient. Before implanting the pulse generator, read the physician's manual carefully.

- When using line-operated electrical equipment during invasive test procedures, the patient must be electrically isolated from potentially hazardous leakage current to prevent inadvertent arrhythmia induction.

*Arrhythmia Conversion Testing*

- If not terminated in a timely fashion, an induced tachyarrhythmia can result in the patient's death. Before tachyarrhythmia induction, both sterile external and internal defibrillator paddles or an equivalent (e.g., R2 pads) must be immediately available and ready for use.

*Avoid Magnetic Resonance Imaging (MRI) in Patients with AICD*

- Keep patients with implanted pulse generators away from MRI devices. Proximity to MRI devices may disable tachyarrhythmia therapy. **Do not subject a patient with an implanted pulse generator to MRI device scanning.** MRI devices contain strong DC magnetic fields that can exert significant mechanical force on an AICD pulse generator because of its ferromagnetic components. Such force may cause physical pain and injury, and may damage the pulse generator. Alternating magnetic fields from MRI procedures may a) cause a pulse generator to charge and deliver a high-voltage shock to the patient, b) inhibit bradycardia pacing, c) disable antitachycardia therapy, or d) change programmed parameters.

## VI. PRECAUTIONS

*Defibrillation*

- External defibrillation has the potential to damage an AICD pulse generator. To help prevent defibrillation damage to the pulse generator, follow these precautionary measures: position defibrillation paddles as far from

the pulse generator as possible; attempt to minimize current flowing through the pulse generator and leads by positioning the defibrillation paddles perpendicular to the implanted pulse generator-lead system; set energy output of defibrillation equipment as low as clinically acceptable; and confirm pulse generator function following any internal or external defibrillation episode (interrogate the device, verify battery status, check the shock counters, and ensure that programmable parameters did not change).

- Use of internal paddles when the AICD pulse generator is connected to the implanted lead system may damage the pulse generator and/or shunt energy. Do not use internal defibrillation unless the pulse generator is disconnected from the leads.

- Successful conversion of ventricular fibrillation or ventricular tachycardia during arrhythmia conversion testing is no assurance that conversion will occur post-operatively. Be aware that changes in the patient's condition, drug regimen, and other factors may change the defibrillation threshold (DFT) which may result in nonconversion of the arrhythmia post-operatively.

***Implantation***

- If a shocking lead impedance using the ECD is less than 20 Ω, the shocking leads should be repositioned to allow a greater distance between the shocking leads. The pulse generator should never be connected to a lead system with less than 15-Ω total impedance. Device damage may result.

- The setscrews should be tightened onto the electrode rings of the rate sensing/pacing lead. If the setscrews are tightened onto the silicone rubber insulation instead of the electrode rings, permanent damage to the lead could occur.

- Do not kink leads. Kinking leads may cause additional stress on the leads, possibly resulting in lead fracture.

***Programming***

- The safety and effectiveness have not been established when a long 1ST-DETECT DURATION (7.5 or 10.0 seconds) is used together with a low 1ST-SHOCK ENERGY (< 15 J). Using this combination of programmed parameters may reduce conversion efficacy.

- If the device is left in STAT PACE settings, these settings may significantly reduce the lifetime of the device.

- Ensure that the pulse generator's TACHY MODE is INACTIVE when not in use, before handling it, and before using electrosurgery.

***Follow-up***

- Noninvasive testing of the pulse generator should be performed only in the presence of medical personnel skilled in cardiopulmonary resuscitation (CPR). In addition, an external defibrillator and a person skilled in its use should be immediately available.

- Advise patients to have their pulse generator checked whenever tones are heard coming from the device.

***Explantation***

- The pulse generator contains sealed chemical power cells and capacitors; **never incinerate a pulse generator**. Be sure that the pulse generator is removed before cremation.

- To prevent unwanted shocks and to preserve device therapy history, program the TACHY MODE to INACTIVE, disable the magnet feature, and disable the AUDIBLE ERI beeper before explanting. **Do not clean**

**or ship the pulse generator unless it has been disabled.**

*Storage*

- Store the pulse generator at temperatures between 0°-50°C (32°-122°F). Allow the pulse generator to reach room temperature before programming or implanting the device.,Store the pulse generator in a clean area, away from magnets, kits containing magnets, and sources of electromagnetic interference (EMI). A "USE BEFORE" date appears on all AICD device packaging. Do not implant the pulse generator after the USE BEFORE date has passed.

*Sterilization*

- CPI sterilizes the pulse generator blister trays and contents with ethylene oxide gas before final packaging. When the pulse generator is received, it is sterile provided the container is intact. If the packaging is wet , punctured, opened, or damaged, return the device to CPI.

- Never attempt to resterilize a VENTAK P2 pulse generator or the wrenches packaged with it. Instead return the pulse generator to CPI.

***Environmental Interference***

***Electromagnetic Sources***

- Electromagnetic interference (EMI) is generated by various sources. Very strong EMI may cause the pulse generator operation to become erratic. Inhibition occurs when the EMI is strong enough to prevent the pulse generator from sensing the patient's intrinsic heart rhythm. Because EMI is typically of a much higher frequency than the patient's heart rhythm, the pulse generator tends to recognize it as noise, and inhibit therapy. Low frequency EMI (e.g., a TENS [transcutaneous electrical nerve stimulator] device) or strong EMI fields may cause the pulse generator to sense incorrectly and deliver inappropriate therapy. Advise patients to avoid sources of EMI wherever possible. Possible electromagnetic sources that could interfere with normal pulse generator operation include the following:

    - Electrosurgical equipment
    - Electrical power sources
    - Arc welding equipment and robotic jacks
    - Electrical smelting furnaces
    - Large RF transmitters such as radar
    - Therapeutic diathermy equipment
    - Electronic surveillance devices (anti-theft devices)
    - Cellular phones (see below)

- Inform patients that they should not lean over an alternator on a car that is running.

- Recent studies have indicated there may be a potential interaction between cellular phones and implantable defibrillator operation. Potential effects may be due to either the radiofrequency signal or the magnet within the phone and could include inhibition or delivery of additional therapies when the phone is within close proximity (within 6 inches) to the pulse generator. It is important to note that any effect resulting from an interaction between cellular phones and implanted pulse generators is temporary. Simply moving the phone away from the implanted device will return it to its previous state of operation. Because of the great variety of cellular phones and the wide variances in patient physiology an absolute recommendation to cover all patients cannot be made. The following information provides a general guideline to patients having an implanted pulse generator who desire to operate a cellular phone. It is important to note that any effect resulting from an interaction between cellular phones and implanted pulse generators is temporary.

- Patients should hold the phone to the ear opposite the side of the implanted device. Patients should not carry the phone in a breast pocket or on a belt over or within 6 inches of the implanted devices as some phones emit signals when they are turned on but not in use (i.e., in the listen or standby mode). Storing the phone in a location opposite the side of implant is recommended.
- Maintain a minimum separation of 6 inches (15 cm) between a handheld personal cellular phone and the implanted device. Portable and mobile cellular phones generally transmit at higher power levels compared to handheld models. For phones transmitting above 3 watts, a minimum separation of 12 inches (30 cm) between the antenna and the implanted device is advised.

***Magnetic Sources***

If the ON/OFF WITH MAGNET feature is programmed ON, the TACHY MODE will toggle between ACTIVE and INACTIVE when the pulse generator is in a strong magnetic field for 30 seconds. Therefore, patients should avoid equipment or situations where they would be exposed to strong (>10 gauss) magnetic fields. The pulse generator emits tones when in a magnetic field that is strong enough to deactivate or activate it.

Possible magnetic sources that could interfere with normal pulse generator operation include the following:

- Industrial transformers
- Industrial motors
- Magnetic resonance imaging (MRI) devices
- Large stereo speakers
- Telephone receivers if held within 0.5 inch (1.27 cm) of the pulse generator
- Radio transmitters, including those used to control toy cars or airplanes
- Magnetic wands such as those used for airport security and in the game "Bingo"

***Other Sources Associated with Patient Care.***

- Proceed as indicated when performing electrosurgery or diathermy and using ionizing radiation:

  - Before using electrosurgery devices, make sure the patient's pulse generator is deactivated. If active, the pulse generator may deliver a shock to the patient. Remember to reactivate the pulse generator after turning off the electrosurgery equipment.
  - Do not subject a patient with an activated implanted pulse generator to diathermy.
  - Ionizing radiation (such as radioactive cobalt, linear accelerators, and betatrons) may adversely affect pulse generator operation, particularly at high doses. Shield the pulse generator during ionizing radiation exposure. Always evaluate the pulse generator's operation after exposure to radiation. Do not project the radiation port directly at the device.
  - Lithotripsy may damage the pulse generator. If lithotripsy must be used, avoid focusing near the pulse generator site.

## VII. POTENTIAL ADVERSE EFFECTS

***Adverse Physical Effects***

Based on the literature and AICD implant experience, the following list includes adverse physical effects from implantation of an AICD pulse generator: acceleration of arrhythmia, air embolism, bleeding, chronic nerve damage, erosion, excessive fibrotic tissue growth, extrusion, fluid accumulation, formation of hematomas or cysts, inappropriate shocks, infection, keloid formation, lead abrasion, lead discontinuity, lead migration/dislodgement, myocardial damage, pneumothorax, shunting current or insulating myocardium during defibrillation with internal or external paddles, potential mortality due to inability to defibrillate or pace, thromboemboli, venous occlusion, and venous or cardiac perforation.

*Adverse Psychological Effects*
Patients susceptible to frequent shocks despite antiarrhythmic medical management may develop psychologic intolerance to an AICD system. Possible psychological effects of implantation of an AICD system include the following: dependency, depression, fear of premature battery depletion, fear of shocking while conscious, fear that shocking capability may be lost, and imagined shocking.

*Other effects*
As with any electronic device implanted in the human body, the AICD pulse generator is subject to random component failure. Such failure could cause inappropriate shocks, induction of arrhythmia or inability to sense arrhythmias, and could lead to the patient's death. Possible pacemaker interaction may occur. Such interaction could result in delivery of inappropriate shocks, delayed therapy, or no therapy at all. Persons administering CPR may experience the presence of voltage on the patient's body surface when the patient's AICD system delivers a shock.

## VIII. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative therapies for the treatment of life threatening ventricular arrhythmias, as deemed appropriate by the physician based upon EP (electrophysiology) testing and other diagnostic evaluation, include the use of antiarrhythmic medication, electrical ablation and cardiac surgery, electronic devices including pacemakers and other commercially available implantable defibrillators or a combination thereof.

## IX. MARKETING HISTORY

In November 1992, Cardiac Pacemakers, Inc. began marketing the VENTAK P2 System outside the United States. The VENTAK P2 has not been withdrawn from marketing in any country for any reason related to the safety or effectiveness of the device. As of August, 1994, over 1700 VENTAK P2 pulse generators have been sold outside the United States. The VENTAK P2 System has been made commercially available in the following countries: Austria, Belgium, Canada, Finland, France, Germany, Greece, Holland, Israel, Italy, Portugal, Spain, Saudi Arabia, Sweden, Switzerland, Turkey, United Kingdom.

## X. SUMMARY OF STUDIES

The non-clinical laboratory (bench) testing provided information relative to the pulse generator, programmer and software module, ECD and leads. The design requirements and specifications were deemed appropriate for these devices.

### A. Component Tests

VENTAK P2 components that were common to CPI families of pulse generators and which were qualified for use in earlier AICD and/or pacemaker applications were not requalified. Previously qualified components include such items as batteries, electrolytic capacitors and standard transistors, diodes, resistors and capacitors. Environmental and accelerated life tests were performed on all very large scale integrated (VLSI) microcircuits used in the VENTAK P2 pulse generator, including the microprocessor, random access memory (RAM), ready only memory (ROM), and custom integrated circuits (ICs). For each test, 25 samples were tested from a production lot. The packaged ICs received electrical parameter tests, temperature stress, hermeticity and other assembly integrity tests. All of the microcircuits were deemed qualified for use in implantable pulse generator applications. Discrete components such as capacitors, the transformer, resistor, and transistors (including insulated gate bipolar transistors [ IGBTs] and metal oxide semiconductor field effect transistors [MOSFETs]) were similarly tested for conformity to

specification requirements and the ability to withstand environmental stresses. Test sample sizes ranged from 15 to 33 components from production or production assembly lots. All of the components were considered qualified for use in implantable pulse generator applications. Hybrid circuit assemblies were subjected to a series of operating life, temperature, process and environmental stress tests. Test samples ranged from 27 to 50 hybrids from production fabricated lots. The High Power modules were also subjected to operating life test. All hybrids were considered qualified for use in implantable pulse generator applications.

**B. Device Tests**

The Model 1625 VENTAK P2 pulse generator was evaluated by electrical, mechanical, electromagnetic interference, firmware, human arrhythmia (tape) and features software testing. The VENTAK P2 pulse generator met all required specifications and demonstrated compatibility with the programmer, software module and other accessories.

- Electrical testing of the pulse generator assembly was performed on a minimum of 6 completed pulse generators and 6 flex assemblies to evaluate rate and electrogram sensing, pace output characteristics, shock output characteristics, telemetry operation and memory retention. Specific tests focused on system characteristics, rate sensing channel, electrogram (shocking) leads sensing channel, R-wave sensing timing, pacing output characteristics, high voltage charging and shock output characteristics, telemetry operation and stress.

- Mechanical testing involved a minimum of 6 pulse generator or case assemblies for each test performed. Tests included audio tone volume, dimensions, weight, top to case bond, top and sealing system, mechanical and thermal shock (physical resistance and memory retention), vibration, magnet actuation distance, ASTM shipping tests and x-ray identifier legibility.

- Electromagnetic interference testing was conducted to assess the response of the pulse generator to electromagnetic interference (EMI). Three devices were tested using conducted interference at an amplitude of up to 100 millivolts for 50 Hz, 60 Hz, 400 Hz, and at 60 Hz magnetic field. Devices were also tested using radiated interference at an amplitude of up to 200 V/m field strength for 450 MHz, 2450 MHz, and 3100 MHz.

- Firmware verification was conducted at each module level with a combination of unit and fully integrated tests to demonstrate proper interaction of the firmware modules/tasks. Recorded arrhythmia evaluations were performed to verify sensing, detection, and event marker functions. Fifty-one recorded human arrhythmias in a select data base were 'played-back' via computer to each of three devices under test. The responses in all cases were in accordance to specification.

- Features (system) testing was performed on VENTAK P2 pulse generator assemblies with the Model 2035 Handheld Programmer and the Model 2835 Software Module to verify proper interaction for the major features of the system including tachy detection, therapy selection, shock delivery, brady sensing, electrophysiology (EP) test mode, support features and memory. Four pulse generators and four programmer software modules were used for testing. Each test was run on one pulse generator programmer combination.

- The Model 2835 Software Module was evaluated for proper operation and interaction with the Programmer and pulse generator. The system tested included the VENTAK P2 pulse generator, the Model 2835 Software Module and the 2035 Handheld Programmer. All software features operated according to the specification requirements.

- Model 2815 ECD underwent hardware/software system verification, electrical verification, and mechanical verification to demonstrate conformance with device specifications.

### C. *Biocompatibility*

The biocompatibility of the tissue contacting materials used in the VENTAK P2 AICD System has been established in previous PMA applications (P890061 and P910078). These materials include: polyurethane, titanium, and silicone rubber which are all currently used in CPI's commercially available devices. No new materials have been introduced.

### D. Animal Studies

A canine study was performed in accordance with "Good Laboratory Practices" regulations per 21 CFR Section 58 to establish the performance of the VENTAK P2 system. Three healthy dogs were implanted with defibrillating patch leads, rate sensing leads and a VENTAK P2, simulating clinical situations that may be encountered. Defibrillation thresholds were measured and electrophysiological testing was performed to evaluate various programmable functions and therapy options. The results demonstrated that the VENTAK P2 AICD system operates properly under simulated test conditions.

### E. Clinical Studies

Two clinical studies were conducted to evaluate the safety and effectiveness of the VENTAK P2 AICD System. The first study, initiated on December 30, 1991 under IDE G910178, was conducted using CPI's conventional patch lead system (requiring a thoracotomy approach). The second study was initiated on October 5, 1992 under IDE G920129, and was conducted using CPI's ENDOTAK 60-Series endocardial lead system.

#### 1. Objectives

The purpose of the clinical investigations was to evaluate the safety and effectiveness of the VENTAK P2 AICD system with both epicardial and endocardial (transvenous) defibrillation lead systems. Within each study, the following general objectives were:

- Demonstrate that the VENTAK P2 can effectively detect and treat ventricular tachy- and brady-arrhythmias.
- Demonstrate that biphasic shocks, as provided by the VENTAK P2, are effective in the termination of ventricular tachyarrhythmias.
- Demonstrate that device diagnostic features and EP tachyarrhythmia induction features operate as designed.
- Demonstrate that the VENTAK P2 pulse generator does not pose an unreasonable risk to patients of morbidity, operative mortality, or device dysfunction.
- Demonstrate that all system components, e.g., pulse generator, leads, VENTAK ECD, programmer and cables, are compatible.

#### 2. Patient Population

***VENTAK P2/Patch Study (G910178) - Thoracotomy Patients***

The VENTAK P2/Patch clinical summary includes information from 320 patients who were implanted with the VENTAK P2 pulse generator and epicardial patch leads using thoracotomy lead implantation techniques. Twenty-nine centers guided by the same investigational protocol, participated in the multicenter study. At the time of the data cutoff (May 26, 1994), 244 patients had been implanted for six months or more and 194 patients had been implanted for twelve months or more.

*VENTAK P2/ENDOTAK Study (G920129) - Nonthoracotomy Patients*

The VENTAK P2/ENDOTAK clinical summary includes information from 610 patients who were implanted with the VENTAK P2 pulse generator and the ENDOTAK 0060-Series Lead System using non-thoracotomy lead implantation techniques. Thirty-nine centers guided by the same investigational protocol participated in the multicenter study. At the time of the data cutoff (May 26, 1994), 454 patients had been implanted for six months or more and 186 patients had been implanted for twelve months or more.

**Table 1. Description of VENTAK® P2 Population**

| Demographic | VENTAK® P2 | VENTAK® P2/ENDOTAK® |
|---|---|---|
| Number of Patients | 320 | 610 |
| Mean age at implant (years) | 62.6 | 61.8 |
| Gender: | | |
| Male | 247 (77.2%) | 480 (78.7%) |
| Female | 73 (22.8%) | 130 (21.3%) |
| Mean LVEF (left ventricular ejection fraction) (%) | 32.6% | 32.4% |
| NYHA (New York Heart Association) | | |
| I | 104 (35.6%) | 171 (31.3%) |
| II | 138 (47.3%) | 260 (47.6%) |
| III | 46 (15.8%) | 107 (19.6%) |
| IV | 4 (1.4%) | 8 (1.5%) |
| Undetermined | 28 | 64 |
| Primary Cardiac Disease*: | | |
| Coronary Artery Disease/Ischemic Cardiomyopathy | 238 (74.8%) | 435 (71.4%) |
| Nonischemic Cardiomyopathy | 52 (16.4%) | 126 (20.7%) |
| Other | 28 (8.8%) | 48 (7.9%) |
| Primary Arrhythmia: | | |
| MVT | 160 (50.0%) | 304 (49.8%) |
| VF | 143 (44.7%) | 241 (39.5%) |
| VT/VF | 17 (5.3%) | 65 (10.75%) |
| Most Common Defibrillating Lead System Configuration | Epicardial Patch/Patch Configuration | ENDOTAK Configuration 3 - Lead alone. |
| Defibrillation Threshold (DFT) | | |
| Mean ± SD (biphasic) | 9.6 ± 6.9 joules | 10.2 ± 5.1 joules |
| Median | 8 joules | 10 joules |

* For two VENTAK P2 patients and one VENTAK P2/ENDOTAK patient primary cardiac disease was not reported.

*Gender Bias Analysis.* The patient inclusion and exclusion criteria were established to avoid gender bias. Of the total 930 patients enrolled in both studies, approximately 78% (727) were male and 22% (203) were female. The ratio of males to females in the VENTAK P2 studies (3.6:1) is similar to the ratio of males to females who have received an AICD worldwide since its inception (4:1), as well as the ratio described in the clinical trials and cohort designs of the Framingham Heart Study (3.8:1) (Cupples, Gragnon, et al., "Long and Short Term Risk of Sudden Coronary Death", Circulation, Vol. 85, No. 1 Supplement I, January

1992; pp. I-11 to I-18.

A separate analysis of safety and effectiveness data indicated no statistical differences between the genders with respect to endpoints influenced by physiology (patient survival, operative mortality, and morbidity). Overall, the following data presented are representative for both men and women.

### 3. Study Design and Comparison Study Group

Patients enrolled in the study were not randomized to receive therapy. The VENTAK® P2 AICD™ System study design used two methodological approaches, epidemiologically described as case series and historical cohort study. The case series method enrolled subjects in phases, so that the performance of the VENTAK® P2 AICD™ System may be observed in smaller number of patients prior to study expansion. The clinical experience gained from the different phases allowed timely changes to the device design and manufacturing as well as appropriate modifications to the protocol.

The historical cohort for the VENTAK® P2 /Patch study is the first 292 patients implanted with the earlier model VENTAK® P AICD™ pulse generators. For the VENTAK® P2 /ENDOTAK® study, the historical cohort is the first 403 patients implanted with the ENDOTAK® 60-series lead system. This cohort of patients was implanted with a mixture of earlier VENTAK® AICD™ pulse generators which consisted of Models 1550, 1555 and Model 1600 (VENTAK® P) AICDs. Potential limitations to these studies exist with the use of historical controls such as biases in patient selection and investigators may be proponents of the therapy under investigation. The major endpoint is patient mortality which is not susceptible to systematic physician bias.

In the final analysis, the control and study groups showed some demographic differences. The VENTAK P2/Patch patients were found to have a higher proportion of patients whose primary cardiac disease was non-ischemic cardiomyopathy, and a higher proportion of patients whose primary arrhythmia was VF than the comparison group. The VENTAK P2/ENDOTAK patients were found to have more patients whose primary cardiac disease was non-ischemic cardiomyopathy than the comparison group. The inclusion criteria do not influence these demographic differences and therefore, these differences are not expected to affect the outcome of the studies. The most important prognostic clinical variables are the left ventricular ejection fraction and the NYHA classification. There is no significant difference between these two later variables between the study groups and the control groups in either case.

### 4. Study Results

*Statistical Analysis*. Descriptive statistics were used to analyze the data gathered in the clinical studies and to summarize results such as frequency distribution, cross tabulations, means, standard deviations, and ranges. Patient survival was analyzed using the life-table (actuarial) methods. Inferential statistics were used, when appropriate, to compare the VENTAK P2 clinical results to the respective comparison groups. For discrete variables Pearson's chi-square or Fisher's exact test were used for statistical analysis of differences between study and comparison groups. For continuous variables, a two sample t-test was used for independent samples, a paired t-test or a Wilcoxon ranked test was used to test for dependent samples in order to test for statistical differences between the study and comparison groups. The appropriate t-test was used, based on the results of the F-test which tests the statistical assumption for the t-test, that the variances are equal. For survival analyses, the Wilcoxon life table analysis was used to test for statistically significant differences between the study and comparison groups.

#### a. Monophasic and Biphasic Shock Comparisons

Biphasic waveform is a new defibrillation waveform found in only one other commercially-available implantable cardioverter defibrillator. To demonstrate that biphasic shocks (as provided by the

VENTAK® P2 AICD™ System) are effective in the termination of tachyarrhythmias, DFT measurements were compared.

**(1) Within Patient Comparisons**

Within patient comparisons were conducted at one investigational center using both monophasic and biphasic waveforms. Testing was performed in a randomized fashion with the lead position constant between waveform DFT evaluations. Eighteen patients in the VENTAK P2/Patch study and nine patients in the VENTAK P2/ENDOTAK were evaluated using both monophasic and biphasic waveforms.

**Table 2. Within Patient Comparisons (DFT Testing Completed Using both Waveforms)**

| | **VENTAK® P2 /Patch n= 18** | **VENTAK® P2 /ENDOTAK® n = 9** |
|---|---|---|
| Waveform | Mean ( ±S.E.) DFT (J) | Mean ( ±S.E.) DFT (J) |
| Monophasic | 12.4 (± 2.1) | 18.1 (± 3.0) |
| Biphasic | 7.4 (± 1.1) | 10.4 (± 2.1) |
| p-value | 0.002 | 0.01 |

**(2) Study Population Comparisons**

True step-down DFT testing is defined as testing in which successively lower energies were tested until an energy level was reached that could not successfully convert VF.

**Table 3. True DFT Testing at Implant for VENTAK® P2/Patch and Comparison Group**

| | **VENTAK® P2 /Patch n= 110** | **VENTAK® P n = 181** |
|---|---|---|
| Waveform | Mean ( ±S.E.) DFT (J) | Mean ( ±S.E.) DFT (J) |
| Monophasic | N/A | 13.2 (± 0.5) Joules |
| Biphasic | 9.6 (± 0.7) Joules | N/A |
| p-value | $p < 0.001$ | |

**Table 4. True DFT Testing at Implant for VENTAK P2®/ENDOTAK and Comparison Group**

| | **VENTAK® P2 /ENDOTAK® n = 352** | **ENDOTAK® n = 271** |
|---|---|---|
| Waveform | Mean ( ±S.E.) DFT (J) | Mean ( ±S.E.) DFT (J) |
| Monophasic | N/A | 16.9 (± 0.3) Joules |
| Biphasic | 10.2 (± 0.3) Joules | N/A |
| p-value | $p < 0.001$ | |

**b. Programmed Parameters**

The programming for new features with the VENTAK P2 pulse generator which were not available in the VENTAK P pulse generator are tabulated below:

**Table 5. Programmed Parameters Usage at 2 Months**

| Parameter | VENTAK® P2 | VENTAK® P2/ENDOTAK® |
|---|---|---|
| VF Protection ON | 76 (28.3%) | 60 (4.7%) |
| Committed Shock = NO | 254 (94.4%) | 442 (93.8%) |
| Polarity = Initial | 268 (99.6%) | 467 (99.2%) |
| Biphasic Waveform | 267 (99.3%) | 467 (99.2%) |
| Brady Pacing = VVI | 244 (90.7%) | 423 (89.8%) |
| Post-shock Pacing = VVI | 263 (97.8%) | 465 (98.7%) |
| Stored EGM* = ON | 269 (100%) | 469 (99.6%) |

* EGM = electrogram

### c. Spontaneous Therapy Efficacy

Information about device efficacy is obtained from therapy history stored within the device. A total of 652 spontaneous episodes of ventricular tachyarrhythmias were recorded in the VENTAK P2/Patch study of which 96.0% were successfully terminated by the device. For the remaining episodes, spontaneous conversions occurred in 3.7% and external rescues occurred in 0.6%.

**Table 6. Spontaneous Therapy for VENTAK® P2/Patch Population**

| Arrhythmia Classification | Number of Episodes | 1st Shock Conversion | Device Conversion |
|---|---|---|---|
| VF/PVT* | 159 | 131 (82.4%) | 157 (98.7%) |
| MVT* | 493 | 399 (80.9%) | 469 (95.1%) |
| Total | 652 | 530 (81.3%) | 626 (96.0%) |

*PVT= polymorphic ventricular tachycardia; MVT= monomorphic ventricular tachycardia

A total of 664 episodes of ventricular tachyarrhythmias were recorded in the VENTAK P2/ENDOTAK study of which 98.5% were successfully terminated by the device. The remaining 1.5% spontaneously converted.

**Table 7. Spontaneous Therapy for VENTAK® P2/ENDOTAK® Population**

| Arrhythmia Classification | Number of Episodes | 1st Shock Conversion | Device Conversion |
|---|---|---|---|
| VF/PVT | 121 | 107 (88.4%) | 120 (99.2%) |
| MVT | 543 | 467 (86.0%) | 534 (98.3%) |
| Total | 664 | 574 (86.5%) | 654 (98.5%) |

### d. Testing Arrhythmia Conversion and Bradycardia Pacing

Other overall study endpoints are summarized in Table 8. These data represent results combined from testing at implant, predischarge and 2 month follow-up visits.

**Table 8. Results during Arrhythmia Conversion and Bradycardia Pacing Testing**

| | VENTAK® P2/Patch Study | VENTAK® P2/ENDOTAK® Study |
|---|---|---|
| Induced Arrhythmia First Shock Conversion Rate | VF/PVT 93.3%<br>MVT 88.6% | VF/PVT 93.6%<br>MVT 96.0% |
| Induced Arrhythmia Device Conversion Rate | VF/PVT 99.2%<br>MVT 99.2% | VF/PVT 99.8%<br>MVT 100% |
| Appropriate Conventional Bradycardia Pacing | 99.50% | 99.90% |
| Appropriate Post-shock Bradycardia Pacing | 99.40% | 99.50% |

**e. Acceleration**

The VENTAK P2 pulse generator measures arrhythmia accelerations as a part of its therapy summary record. The pulse generator defines an acceleration as a rhythm that is initially detected above the lower rate cutoff and below the VF Protection rate cutoff which is subsequently detected above the VF Protection rate cutoff following the first shock.

Accelerations occurred in seven (7, 1.0%) of the 668 spontaneous and induced episodes during the course of the VENTAK P2/ENDOTAK investigation. All seven (7, 100.%) accelerations were converted with the second shock. Out of 1054 induced and 798 spontaneous episodes, accelerations occurred in seven (7, 0.4%) episodes in the VENTAK P2/Patch study. Six episodes were converted with the second shock and one episode was converted by a third shock.

**f. Clinical Events (Observations and Complications)**

Complications are defined as "A clinical event that cannot be treated or resolved by reprogramming the device and requires intervention." Observations are defined as "An asymptomatic or symptomatic clinical event with potential adverse effects that does not require intervention and can be corrected by programming or simple adjustments.

**Table 9. VENTAK® P2 Study Distribution of Clinical Events**

| Category | VENTAK® P2/Patch | | VENTAK® P2/ENDOTAK® | |
|---|---|---|---|---|
| | Number | Percent of Total | Number | Percent of Total |
| Therapy Delivery | 73 | 65.8% | 105 | 46.7% |
| Detection | 16 | 14.4% | 46 | 20.4% |
| Physiologic | 9 | 8.1% | 24 | 10.7% |
| Diagnostics | 11 | 9.9% | 27 | 12.0% |
| System Components | 2 | 1.8% | 23 | 10.2% |
| TOTAL | 111 | 100.0% | 225 | 100.0% |

Five categories were used to report clinical events noted during the clinical studies: (1) Therapy Delivery - which included events such as inappropriate therapy, inability to convert, loss of capture and delayed therapy; (2) Detection - which included events such as non-detection, oversensing and undersensing; (3) Physiologic - which included events related to infection, erosion, hematoma, pericardial effusion and

altered hemodynamic status; (4) Diagnostics - which included events related to battery status indicators, EP test function and difficulty with therapy history recording; and (5) System Components - which included events related to external component interface such as difficulty with programming, interrogating, printing and inability to obtain event markers. Table 9 summarizes the distribution of clinical events.

Of the total clinical events reported, the majority of events related to therapy delivery (66% and 47% respectively). In particular, the majority of these events were due to the delivery of inappropriate shocks due to supraventriculr arrhythmias being detected above the rate cutoff. In the VENTAK P2/ENDOTAK study, there were 14 observations of delayed therapy where the device sensed two slow beats and inhibited the delivery of the shock. In all cases, the subsequent detection sequence delivered a committed shock.

**g. Patient Survival**

Mortality was the primary endpoint designated for both studies. To demonstrate that the VENTAK® P2 AICD™ System can effectively detect and treat ventricular tachyarrhythmias and bradyarrhythmias, the life table actuarial method was used to examine patient survival. Patient survival was analyzed for 'all cause' mortality, sudden cardiac death and total cardiac death. The effective sample size, which is the number of patients analyzed at a given timeperiod (taking statistical censoring rules into account) is presented with survival statistics.

**Table 10. Survival Data at 12 Months**

| Survival Category | VENTAK® P2 /Patch | VENTAK® P (P890061) Historical Control Group | VENTAK® P2 /ENDOTAK® | ENDOTAK® (P910073) Historical Control Group |
|---|---|---|---|---|
| Total 'All Cause' Survival | 92.5 ± 1.6% (186.5) | 89.2 ± 1.8% (251.5) | 94.1 ± 1.2% (178.5) | 90.4 ± 1.6% (176.5) |
| | p = 0.15 | | p = 0.047 | |
| Sudden Cardiac Death Survival | 98.3 ± 0.9% (186.5) | 98.2 ± 0.8% (250.5) | 97.8 ± 0.7% (178.0) | 97.4 ± 0.9% (176.0) |
| | p = 0.79 | | p = 0.95 | |
| Total Cardiac Survival | 95.5 ± 1.2% (186.5) | 93.3 ± 1.5% (251) | 96.9 ± 0.9% (178.5) | 92.4 ± 1.4% (176.5) |
| | p = 0.30 | | p = 0.01 | |

The Wilcoxon test was used to test for statistically significant differences between groups. There were no deaths censored from the analysis, even if the device was deactivated at the time of death. There were no significant differences between the VENTAK P2/Patch population and the VENTAK P comparison group. There were significant differences in total cardiac survival and from all causes of death in favor of the VENTAK P2 /ENDOTAK population.($p < 0.05$), otherwise, no statistical differences were found with respect to sudden cardiac death ($p > 0.05$).

An analysis based on "intention to treat" showed that there was no difference in survival between the comparison groups and all patients enrolled in the clinical investigation. A subanalysis of the deaths within the first 30 days (operative mortality) accounted for 5 of 27 deaths in the VENTAK P2/Patch population

and 6 of 30 deaths in the VENTAK P2/ENDOTAK population. These numbers accounted for 1.6% and 1.0%of the total patients implanted.

## XI. DEVICE ACCOUNTABILITY, RELIABILITY AND LONGEVITY

Table 11 provides a summary of all VENTAK P2 pulse generators utilized in the VENTAK P2 clinical investigations, including devices from attempted implants, patients in each study population, patients with lead configurations other than those recommended in the study protocol, emergency use patients, and patients who received a replacement VENTAK P2.

**Table 11. Device Accountability**

| | **VENTAK® P2/Patch** | **VENTAK® P2/ENDOTAK®** |
|---|---|---|
| Devices Used:<br>Implanted (Attempted) | 374<br>367 (7) | 678<br>677 (1) |
| Devices Implanted:<br>Active/ Inactive Mode<br>Monitor Mode<br>Lost to follow-up<br>Out-of-service | (367)<br>307/ 0<br>1<br>2<br>57 | (677)<br>598/ 3<br>0<br>16<br>60 |
| Out-of Service Devices: | (57) | (60) |
| Due to Deaths<br>Not Returned<br>Met Specifications<br>Faults/Damage Induced During explants | (31)<br>12<br>18<br>1 | (33)<br>15<br>15<br>3 |
| ERI Reached<br>Met Specifications<br>Premature Battery Depletion<br>Digital Hybrid Damage<br>Not Returned | (17)<br>12<br>3<br>1<br>1 | (2)<br>1<br><br>1 |
| Heart Transplant<br>Met Specifications<br>Not Returned | (3)<br>2<br>1 | (5)<br>4<br>1 |
| Infection (MES*) | 2 | 13 |
| Inappropriate Therapy (Oversensing) | 2 | 3 |
| Set screw problem (MES*) | 1 | 3 |
| Short circuit (patch leads touching)<br>damaged output bridge | 1 | |
| Multiple non-sustained events (MES*) | | 1 |

* MES = met electrical specification which is defined as having successfully completed a series of electrical tests covering all pulse generator functions.

Manufacturing process changes were implemented to address the incidents of digital hybrid damage noted in a small number of devices. The digital hybrid damage was found to be caused by electrical overstress resulting from the piezo attachment process. No additional instances of digital hybrid damage have been reported since implementation of the manufacturing changes. Device circuitry changes were implemented early in the clinical study to restore the device longevity to its original estimate of approximately 4 years. The clinical data for devices implanted with the modified circuitry supports the estimated longevity cited in the Physician's Manual.

The overall reliability of the VENTAK P2 pulse generator is expected to be 0.11% per month based on MIL-STD-217. Actual reliability as calculated from clinical data has been determined to be 0.10% per month. When accounting for the resolution of the digital hybrid issue, the reliability is recalculated as 0.06% per month.

## XII. CONCLUSIONS DRAWN FROM THE STUDY

In vitro testing consisted of component level testing, device testing and system testing. Simulated human arrhythmia testing as well as in vivo animal testing also demonstrated the VENTAK P2 AICD System could detect and treat tachyarrhythmias. These tests provided reasonable assurance that the VENTAK P2 pulse generator and other system components were reliable and safe prior to initiation of the clinical studies. The results of the clinical studies provide reasonable assurance that the VENTAK P2 AICD System is safe and effective when it is used as indicated in the labeling.

## XIII. FDA DECISION

On October 27, 1994, FDA completed an inspection of CPI's manufacturing facilities (St. Paul, MN) and determined that the manufacturer was in compliance with the Device Good Manufacturing Practices Regulation (21 CFR part 820).

After the first 55 devices were implanted in 54 patients (G910178), clinical results from this Phase I study and recommendations from the clinical investigators resulted in design modifications to the device. The primary reason was to improve the device performance at low battery voltages. The design changes that took place required modifications to Model 2835 Software Module (Revision 4.1). The charging voltage threshold was reduced to prevent the premature tripping of ERI since modification to the charging circuits could not be implemented on these devices. An automatic weekly check was also added to monitor battery voltage.

For the new devices (post-Phase I G910178 and all G920129 pulse generators), firmware Revision 5.0 was implemented. The important modifications to the new VENTAK P2 devices included modification to the charging circuit to reduce charging current, automatic reformation of high voltage capacitors at 60 days, and modification to the reconfirmation algorithm as well as several minor enhancements such as changes in nominal values (EGM electrogram storage - ON, committed shock - NO).

In September 1993, CPI recalculated the device longevity predictions based on manufacturing data. Based on these estimates, the longevity predictions in the Physician's Manual were revised. These predictions were verified based on analysis of the clinical data obtained with Phase II devices. The longevity prediction (approximately between 2.9 to 4.6 years) was calculated to be comparable or longer than the labeled longevity for the commercially available VENTAK P and VENTAK PRx AICDs.

FDA also consulted with members of the Circulatory System Devices Panel, an FDA advisory Panel, on the clinical aspects. On February 13, 1995 at FDA's request, FDA and CPI convened a meeting at FDA to address all remaining engineering and clinical issues. In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

On March 1, 1995, FDA issued an approvable letter. On March 6, 1995, Cardiac Pacemakers, Inc. submitted an amendment to the application providing the information required by FDA.

FDA approval is subject to the applicant's compliance with the "Conditions of Approval for Implantable Defibrillators and Programmers" (Attachment A), and the conditions that the sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

## XIV. APPROVAL SPECIFICATION

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the following information: (1) updated life testing conducted on the pulse generator's power source (battery) and high energy capacitors; (2) updated details of any patients with devices confirmed to exhibit digital hybrid damage due to electrical overstress resulting from the piezo attachment process; (3) updated calculations of device longevity based on further clinical experience; and, (4) updated analysis of survival for patients programmed with 'VF Protection' ON and OFF.